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Longitudinal changes in weight in relation to smoking cessation in participants of the EPIC-PANACEA study

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Abstract: PURPOSE: We assessed the association between smoking cessation and prospective weight change in the European population of the European Prospective Investigation into Cancer and Nutrition-Physical Activity, Nutrition, Alcohol, Cessation of smoking, Eating out of home And obesity (EPIC-PANACEA) project. METHODS: The study involved more than 300,000 healthy volunteers, recruited between 1992 and 2000 in 9 European countries, who provided data on anthropometry and smoking habits at baseline and after a follow-up of 5years on average. Adjusted mixed-effects linear regression models were used to obtain sex-specific summary estimates of the association between the change in smoking status and the annual change in weight. RESULTS: Smoking cessation tends to be followed by weight gain; when compared to stable smokers, annual weight gain was higher in men (0.44kg (95%CI: 0.36; 0.52)) and women (0.46kg (95%CI: 0.41; 0.52)) who stopped smoking during follow-up. When smokers who stopped smoking at least 1year before recruitment were compared to never smokers, no major differences in annual weight gain were observed. The excess weight gain following smoking cessation appears to mainly occur in the first years following the cessation. CONCLUSIONS: When considering the benefits of smoking cessation, such findings strengthen the need for promoting cessation offering information on weight gain control and support to weight-concerned smokers in order to remove a barrier to quitting.

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Abstract

Purpose

We assessed the association between smoking cessation and prospective weight change in the European population of the EPIC-PANACEA project.

Methods

The study involved more than 300,000 healthy volunteers, recruited between 1992 and 2000 in 9 European countries, who provided data on anthropometry and smoking habits at baseline and after a follow-up of five years on average. Adjusted mixed-effects linear regression models were used to obtain sex-specific summary estimates of the association between the change in smoking status and the annual change in weight.

Results

Smoking cessation tends to be followed by weight gain; when compared to stable smokers, annual weight gain was higher in men (0.44 kg (95%CI: 0.36; 0.52)) and women (0.46 kg (95%CI: 0.41; 0.52)) who stopped smoking during follow-up. When smokers who stopped smoking at least one year before recruitment were compared to never smokers, no major differences in annual weight gain were observed. The excess weight gain following smoking cessation appears to mainly occur in the first years following the cessation.

Conclusions

When considering the benefits of smoking cessation, such findings strengthen the need for promoting cessation offering information on weight gain control and support to weight-concerned smokers in order to remove a barrier to quitting.

List of abbreviations and acronyms:

BMI: Body Mass Index

EPIC-PANACEA: European Prospective Investigation into Cancer and Nutrition–
Physical Activity, Nutrition, Alcohol, Cessation of smoking, Eating out of home And
obesity

SD: Standard Deviation

CI: Confidence Interval

Introduction

Obesity is one of the greatest public health challenges of the 21st century. Because obesity leads to serious health consequences such as cardiovascular diseases, diabetes, musculoskeletal disorders and some cancers(World Health Organization, 2006; World Health Organization, 2007; Kelly et al., 2008), reducing and preventing obesity is an urgent public health goal. At the same time, tobacco use remains the leading cause of preventable death worldwide today(World Health Organization, 2009) and therefore is an issue that still needs to be highly and urgently addressed. While obesity and tobacco smoking have independent considerable hazardous effects on morbidity and mortality, the double burden of obesity and smoking has been shown to have a major impact on health. When compared to non smokers of normal weight, obese smokers showed a 13-year decrease in life expectancy(Peeters et al., 2003). Previous studies also showed that tobacco smoking and obesity are interrelated: current smokers on average weigh less than never smokers(Flegal et al., 1995; Molarius et al., 1997; Travier et al., 2009), former smokers tend to weigh more than smokers(Flegal et al., 1995; Molarius et al., 1997; Filozof et al., 2004; Travier et al., 2009) and never smokers(Flegal et al., 1995; Molarius et al., 1997; Filozof et al., 2004), and BMI is positively associated with smoking intensity in current smokers(Laaksonen et al., 1998; Chiolero et al., 2007; Travier et al., 2009) but negatively associated with time since quitting in former smokers(Flegal et al., 1995; Travier et al., 2009). Since the fear of gaining weight might be an important barrier to quit smoking, a better understanding of this complex relationship is needed. Recent longitudinal studies indicated that the excess weight gain following smoking cessation is probably transient and tends to occur shortly after cessation(Reas et al., 2009; Basterra-Gortari et al., 2010) but large scale studies are required to confirm these findings.

To investigate the relation between smoking cessation and prospective weight change, we used the European Prospective Investigation into Cancer and Nutrition–Physical Activity, Nutrition, Alcohol, Cessation of smoking, Eating out of home And obesity (EPIC-PANACEA) study.

Materials and methods

Population

EPIC is an ongoing multi-centre, prospective cohort study investigating the role of biomarkers and metabolic, dietary and lifestyle factors in the development of cancer and other chronic diseases. The methods of this study have been reported in full by Riboli *et al.* (Riboli et al., 2002). In brief, 521,448 men and women, mostly aged 35 to 70 years, were mainly recruited between 1992 and 2000 from the general population in 23 centres from 10 European countries (Denmark, France, Germany, Greece, Italy, Netherlands, Norway, Spain, Sweden, and United Kingdom). Exceptions were the cohorts of France based on health insurance members; components of the Italian and Spanish cohorts including blood donors; the cohorts from Utrecht (Netherlands) and Florence (Italy) that comprised participants of breast cancer screening programs; and the cohort from Oxford (United Kingdom) that consisted of health-conscious individuals. In France, Norway, Utrecht (Netherlands), and Naples (Italy), only women were included. Approval for this study was obtained from the ethical review boards of the International Agency for Research on Cancer as well as from all institutions where participants had been recruited. Eligible subjects who accepted to participate signed an informed-consent agreement and received by mail a diet and a lifestyle questionnaire. Updated information on lifestyle and anthropometry were obtained from EPIC participants through follow-up questionnaires.

From the 521,448 subjects initially recruited, we excluded 23,713 participants with missing dietary and non-dietary questionnaires, missing data on weight and height at baseline or with extreme or implausible anthropometric values, pregnant women, and those with an extreme ratio of energy intake to estimated energy requirement. We further excluded 123,932 participants for whom weight at follow-up was not available (n=121,866; this included the cohorts of Turin and Ragusa (Italy) and parts of the cohorts from Norway and Naples (Italy)) or with extreme weight changes (weight change <-5 or >5 kg/year). More details on exclusions have been previously published (Romaguera et al., 2010). Finally, from the 373,803 remaining participants, we excluded those for whom information on cigarette smoking was missing at recruitment or at follow-up (n=44,412), and in particular, the centres of Greece and Varese (Italy) because these did not include information on smoking status at follow-up reducing the study sample to 329,391 individuals.

Anthropometric measurements

Recruitment anthropometric measurements were obtained using similar standardised procedures in most centres except those of Oxford (United Kingdom), France and Norway where self-reported anthropometric values were used (Haftenberger et al., 2002). To reduce heterogeneity related to the clothing worn during measurement, corrections of -1.5 kg and -1.0 kg were respectively adopted for subjects who did not wear shoes but were normally dressed and for subjects in light clothing. In Oxford, sex- and age-specific anthropometric values were predicted from participants with both measured and self-reported body measures using linear regression models (referred to as Oxford correction equations in the remainder of the article) (Spencer et al., 2002). BMI was calculated as weight (kg) divided by height (m) squared. At follow-up, weight was self-reported except in Cambridge (United Kingdom) and Doetinchem (Netherlands) where weight was measured and adjusted to take into account clothing worn during

measurement. The Oxford correction equations (Spencer et al., 2002) were applied to all self-reported weights (both at recruitment and follow-up) in order to predict measured weight and calculate corrected weight change. As follow-up time differed across centres our main outcome was annual weight change in kg/year.

Tobacco smoking

At recruitment, detailed information on smoking was collected but much shorter questionnaires were used at follow-up and most participants were only asked to provide their smoking status (never, former, current). Smoking status at recruitment and follow-up were combined to create a nine category variable. Three categories were defined by participants who had the same status at recruitment and follow-up (stable): never-never (48% of the population), former-former (25%) and current-current (16%). Among the participants who changed their smoking habits, we identified those who started to smoke (never – current, 1% of the population), those who relapsed (former – current, 2%), those who quitted (current – former, 5%) and those who started and then quitted (never – former, 2%). Beside these groups, we also had two groups of former (n=5,915; 1.8%) and current (n=1,061; 0.3%) smokers at recruitment who identified themselves as never smokers at follow-up. These incorrect data that may reflect recall issues, differences in the definition of smoking or coding errors were excluded from the present study which includes 322,415 individuals. While stable never smokers defined the reference group in most analyses, quitters were compared to stable current smokers. Smoking intensity (<20 or ≥20 cig/day at recruitment) and time since smoking cessation (≤1, 1.1 to 5 and >5 years before recruitment) were also taken into account.

Other covariates

The educational level, based on the highest school level reached was used as a proxy for socioeconomic status. To adjust for physical activity, we used a validated

index (inactive, moderately inactive, moderately active, active, missing)(Wareham et al., 2003) combining work and leisure time activities. The information on alcohol consumption, that reflected the amount of alcohol consumed daily during the 12 months prior to recruitment, was summarized into a seven level variable for men (0, >0 to ≤ 6 , 7-18, 19-30, 31-60, 61-96, >96g/day) while for women the highest two categories were combined. Total energy intake was computed from the food frequency questionnaire. A binary variable was used to distinguish peri- and post-menopausal women from premenopausal women at recruitment.

Statistical methods

Analyses were carried out separately for men and women. The association between smoking and annual weight change was first estimated within each country. Linear models were run for the countries with only one centre, whereas mixed-effects linear models with random intercept at centre level were used for the others. Multilevel mixed-effects linear regression models with random intercepts and slopes were used to obtain summary estimates. These models allow the country and centre effects (intercepts) but also the effects of smoking to be random and therefore to differ across countries and centres while taking into account the clustering of the data in three levels (individuals, centres, countries). The heterogeneity across countries was assessed using a random effect meta-analysis of the country specific estimates.

We report on weight changes in the stable groups and in quitters and starters, but individuals who relapsed or started and quit during follow-up were included in the models along with potential confounders such as age at recruitment (years), energy intake (kcal/day), education, physical activity, alcohol consumption, menopausal status and weight at recruitment.

We performed analyses stratified for BMI at recruitment and for follow-up time and tested the interaction using log-likelihood ratio tests. The same tests were used to compare the models with and without follow-up time.

In addition to the relative effects, we computed adjusted means of weight change for the different smoking categories corrected for self-reporting applying the “Oxford correction equations”(Spencer et al., 2002) to all participants with self-reported weight to predict their likely measured weight and calculate the corrected weight change. Applying this correction on self-reported weight did not modify relative effects.

Finally, we studied the association between smoking cessation and the likelihood of becoming obese after 5 years of follow-up in participants who were not obese at recruitment (BMI<30, n=284,723). Logistic regressions adjusted for the confounders previously mentioned were performed for each country and were later combined using random-effect meta-analysis to provide sex-specific summary estimates. All statistical analyses were performed with *Stata* software version 10.0.

Results

The final analyses included 322,415 participants; among them 9.47% changed their smoking status over an average follow-up time of 4.98 years (Standard Deviation (SD): 2.06). Descriptive characteristics of the participants stratified by sex and smoking status at recruitment and follow-up are shown in Table 1. On average, the annual increase in body weight was of 0.06 kg (SD: 1.02) in men and 0.22 kg (SD: 1.01) in women, but became of 0.45 kg (SD: 1.00) in men and 0.42 kg (SD: 1.00) in women after correcting for self-reporting.

Annual weight gains ranging from 0.36 kg to 1.12 kg were observed in all the groups defined by smoking status at recruitment and follow-up (Table 2). Among the participants who did not change their smoking status during follow-up, no major

differences in annual weight change were observed when stable current or stable former smokers were compared to stable never smokers, although annual weight gain in male stable former smokers was slightly higher than in stable never smokers ($\beta=0.05$; 95%CI: 0.03; 0.07) and annual weight gain in female stable current smokers was slightly lower than in stable never smokers ($\beta=-0.06$; 95%CI: -0.07; -0.05). The significant increase observed in male stable former smokers when compared to stable never smokers was mainly due to former smokers who stopped one year or less before recruitment. Among stable former smokers, the median time since quitting (from cessation to recruitment) was 15 years and the groups of stable former who stopped a year or less and from 1 to 5 years before recruitment represented respectively 3% and 14% of stable former smokers. When compared to stable current smokers, quitters showed higher weight gains ($\beta=0.44$; 95%CI: 0.36; 0.52 for men and $\beta=0.46$; 95%CI: 0.41; 0.52 for women) and the differences were even more pronounced for heavy smokers at recruitment (20 cig/day or more).

Country-specific annual changes in weight for quitters when compared to stable current smokers showed heterogeneous results in both men and women, nevertheless, all estimates showed a significant weight gain (figures 1 and 2). When stable former smokers were compared to stable never smokers, even if homogeneity was rejected in women, the results were consistent and showed a marginally significant weight gain in men and no significant differences in women (figure 3 and 4).

The analyses stratified by BMI at recruitment showed that in men the association between smoking cessation and weight change was modified by BMI at recruitment. When compared to stable current smokers from the same BMI category, normal weight males quitters gained more weight ($\beta=0.57$; 95%CI: 0.43; 0.72) than obese male quitters ($\beta=0.32$; 95%CI: 0.20; 0.44) (p-value for interaction: 0.014) (data not shown in a table).

On the other hand, adjusting or stratifying for follow-up time or adjusting for BMI at recruitment rather than weight did not change the main results previously presented.

Among the participants classified as non-obese (BMI<30) at recruitment, when we compared quitters to stable current smokers we observed that the Odds Ratios (OR) of becoming obese were 2.27 (95%CI 1.85; 2.78) and 2.84 (95%CI 2.42; 3.34) in men and women respectively. When stable former smokers were compared to never smokers, OR of 1.34 (95%CI 1.22; 1.48) and 1.02 (95%CI 0.96; 1.08) were respectively observed in men and women (data not shown in a table).

Discussion

This study shows significant annual differences in weight gain between quitters and stable smokers of about 0.44 kg and 0.46 kg in men and women, respectively. Nevertheless, when smokers who stopped smoking at least one year before recruitment were compared to never smokers, no major differences in annual weight gain were observed. While never smokers showed annual weight gains of 0.40 kg and 0.43 kg in men and women respectively, men and women who stopped smoking 1 to 5 years before recruitment showed annual weight gains of 0.48 kg and 0.47 kg respectively and both men and women who stopped more than 5 years before recruitment showed annual weight gains of 0.44 kg.

The major strengths of this study include its prospective design, its large size, its reliance on a general population sample and the availability of several potential confounders. Being able to assess weight changes in participants who stopped smoking during follow-up as well as before recruitment, and therefore compare the effects of short and long term abstinence is another strength of this study. Nevertheless, not knowing the sequence of the changes that occurred during follow-up is a limitation to assess causality, as either change could have arisen first and caused the other. Another

limitation of the study is the use of self-reported weight since measured anthropometric values were only obtained for 68% of the population at baseline and for 6% of the population at baseline and follow-up. However, while self-reported weight tend to be underestimated(Gorber et al., 2007), strong correlations have been observed between self-reported weight and measured weight(Spencer et al., 2002). In addition, the use of the Oxford correction equations(Spencer et al., 2002) on self-reported weight, that provided an average corrected weight gain similar to the one observed in the two centres that had measured data at recruitment and follow-up (Cambridge (United Kingdom) and Doetinchem (Netherlands)), allowed us to improve the accuracy of weight change adjusted means. The lack of information on the use of weight-loss diets during follow-up in all participants, and in particular in quitters, also needs to be mentioned as a limitation since this may have affected weight changes. Finally, respondents (81%) and non-respondents to the second weight assessment were compared, and the main determinants of the response rate were follow-up time and recruitment strategy that differed across centres (more details in Romaguera et al. (Romaguera et al., 2010)).

The higher weight gain observed in quitters compared to stable smokers was expected and corroborates findings of previous longitudinal studies(Pisinger and Jorgensen, 2007a; Sneve and Jorde, 2008; Reas et al., 2009; Munafo et al., 2009; Basterra-Gortari et al., 2010; Kimokoti et al., 2010). The present study also assessed the risk of becoming obese after smoking cessation and showed that when compared to stable current smokers, quitters are two to three times more likely to become obese. While further research is still needed to increase the understanding of underlying biological mechanisms, changes in food preference and increased caloric intake, decreased resting metabolic rate and physical activity and changes in adipose tissue metabolism seem to be among the most plausible explanations(Ferrara et al., 2001; Filozof et al., 2004; Chatkin and Chatkin, 2007; Chiolero et al., 2008; Pistelli et al., 2009; Berlin, 2009). While there is a large body of evidence supporting an increase in

body weight following smoking cessation, there is still controversy regarding the magnitude of this weight gain. In the present study, quitters showed a 5-year weight gain of 2.8 kg on average and only 5% of them gained more than 12 kg over a 5-year period. This weight gain is similar to the gain observed in an English cohort of males aged 45-59 years interviewed 4 times over a 15-year period of time(Munafo et al., 2009), but slightly higher than the gain observed in the Spanish SUN cohort(Basterra-Gortari et al., 2010). In this young cohort with a 4-year follow-up, the difference in weight between quitters and continued smokers did not exceed 1.5 kg in both men and women(Basterra-Gortari et al., 2010). The observed differences in magnitude may reflect differences in follow-up time and the fact that the shortest studies tend to report the highest annual weight gains supports the idea that most weight gain probably occurs in the first years following cessation, a critical period for potential relapse. The positive association observed between smoking intensity before cessation and weight gain after cessation corroborates the results of a Norwegian study(Sneve and Jorde, 2008). This finding is very important and needs to be taken into account since significant weight gain may lead to smoking relapse. Although Peto *et al.* showed that smoking cessation leads to a gain in life expectancy far more important than what a smoker could expect to gain from weight control(Peto et al., 2010), if weight gain increases the risk of relapse, reducing weight gain in order to decrease the probability of relapse is a priority, especially in heavy smokers as this group is the group who will benefit the most from smoking cessation.

Previous studies observed gender specific patterns in weight gain following smoking cessation. While Reas *et al.* found that men who stopped smoking 5 or less years before the end of follow-up showed weight gains higher than women (5.1 kg and 2.6 kg, respectively)(Reas et al., 2009), Pisinger and Jorgensen showed that one year after smoking cessation women had gained more weight than men(Pisinger and Jorgensen, 2007b). No strong gender pattern was observed in the present study. On the

other hand, our study tends to show that weight gain following smoking cessation might differ according to BMI at recruitment, and might in particular be lower in obese quitters. Because weight was mainly self-reported at follow-up, this result needs to be interpreted with caution as underreporting at follow-up might have differentially biased the results.

Our analyses comparing stable former and never smokers confirm that after achieving long-term abstinence former smokers show annual increases in weight roughly equivalent to those observed in never smokers. This probably means that the mechanisms contributing to the increase in body weight associated with smoking cessation might be limited to the first years following abstinence. This hypothesis is strengthened by the fact that stable current and never smokers experience similar annual weight gain, indicating no important long-lasting metabolic or lifestyle effects in smokers. Therefore, in order to avoid weight gain that may lead to unsuccessful quitting attempts, weight issues might be addressed before or in the early stages of smoking cessation. A recent review concluded that adding weight control to smoking cessation treatment did not undermine either short- or long-term smoking abstinence and provided significant evidence for short-term benefit for both abstinence and weight control(Spring et al., 2009). Combining smoking treatment and behavioural weight control might be one of the ways to get rid of one of the major barriers to quit smoking. Since physical activity(May et al., 2010; Ekelund et al., 2011) and healthy diet(Mendez et al., 2006; Pisinger and Jorgensen, 2007a; Vergnaud et al., 2010; Romaguera et al., 2010; Beunza et al., 2010) were shown to help in reducing the risk of abdominal and general obesity in this population, intervention studies promoting physical activity as well as a healthy diet in combination with a smoking cessation programme may provide integrated tools to achieve the goal of reducing smoking prevalence while avoiding post cessation weight gain.

Conclusions

This study confirms that smoking cessation tends to be followed by weight gain but also indicates that the excess gain observed in quitters seems to mainly occur during the first years following cessation. When compared to the benefits of smoking cessation, such findings strengthen the need for promoting smoking cessation while offering information and support to smokers, in order to control their weight following cessation and therefore remove this barrier to quit smoking.

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Table 1. Descriptive characteristics of EPIC participants according to their smoking status at recruitment, between 1992 and 2000, and after a follow-up of 5 years on average (mean and standard deviation unless otherwise stated)^a.

	Stable never (n=28,991)	Stable former (n=30,463)	Stable current (n=18,443)	Quitter (n=5,858)	Starter (n=686)	Relapse (n=1,925)	Never-Former ^b (n=1,182)
Men (n=87,548)							
Age at recruitment (year)	51.21 (10.25)	55.23 (8.65)	51.97 (8.26)	52.85 (8.49)	45.18 (10.84)	50.08 (8.93)	50.30 (11.17)
Height at recruitment (cm)	175.69 (7.24)	175.15 (7.03)	174.71 (7.34)	175.35 (7.22)	176.03 (8.06)	175.29 (7.26)	175.19 (7.48)
Weight at recruitment (kg)	80.12 (11.38)	82.39 (11.48)	80.49 (11.82)	80.94 (11.63)	81.77 (12.56)	83.81 (11.46)	79.02 (11.54)
BMI at recruitment (kg/m ²)	25.97 (3.46)	28.66 (3.41)	26.39 (3.69)	26.33 (3.53)	26.42 (3.87)	27.31 (3.60)	25.77 (3.61)
Energy intake (Kcal)	2400.2 (640.10)	2387.6 (629.68)	2567.1 (670.61)	2480.7 (652.88)	2481.2 (700.08)	2490.6 (687.51)	2325.6 (663.49)
Annual weight change (kg)	0.07 (0.94)	0.03 (1.01)	-0.01 (1.04)	0.44 (1.16)	0.16 (1.03)	-0.20 (1.20)	0.12 (0.99)
Corrected weight change (kg) ^c	0.45 (0.92)	0.41 (1.00)	0.41 (1.04)	0.84 (1.14)	0.53 (0.98)	0.22 (1.18)	0.54 (0.97)
School level (%)							
None	3.4	2.9	6.1	4.3	7.4	5.2	7.1
Primary	21.6	26.8	33.5	29.7	18.4	25.7	17.4
Technical/Professional	22.9	26.3	25.4	26.4	22.3	23.8	18.4
Secondary	14.4	11.4	11.5	11.6	21.4	12.7	12.4
University	34.4	28.2	21.5	25.8	28.4	29.7	36.6
Not specified	3.2	4.3	2.0	2.2	2.0	2.9	8.0
Alcohol consumption (%)							
0 g/day	6.3	5.7	6.3	5.4	2.9	6.3	5.9
1-6 g/day	29.1	19.2	15.1	18.6	26.8	17.4	34.2
7-18 g/day	32.2	30.3	23.8	26.6	30.2	27.3	32.2
19-30 g/day	14.3	17.1	15.3	17.1	12.2	16.0	9.9
31-60 g/day	13.8	20.4	23.5	21.6	18.4	23.2	12.9
61-96 g/day	3.3	5.7	11.1	8.6	6.6	6.9	4.0
>96 g/day	0.9	1.5	4.8	2.1	2.9	3.1	0.9
Physical activity (%)							
Inactive	13.4	17.1	17.3	17.0	8.3	13.2	15.7
Moderately inactive	27.6	30.4	28.7	29.5	20.8	28.6	28.4
Moderately active	22.1	23.1	22.9	23.2	22.0	21.9	20.2
Active	23.1	23.8	25.2	22.1	20.8	28.0	19.5
Missing	13.8	5.5	5.9	8.1	28.0	8.2	16.2
Women (n=234,867)							
Age at recruitment (year)	52.00 (9.18)	51.78 (8.81)	49.53 (8.45)	49.65 (9.03)	47.98 (9.11)	47.41 (8.77)	49.88 (10.46)
Height at recruitment (cm)	162.03 (6.49)	163.71 (6.19)	163.52 (6.35)	164.06 (6.40)	162.70 (6.19)	164.10 (6.38)	162.83 (6.20)
Weight at recruitment (kg)	64.97 (11.27)	66.17 (11.52)	64.76 (11.05)	65.33 (11.13)	61.98 (9.97)	66.35 (11.30)	63.37 (10.71)
BMI at recruitment (kg/m ²)	24.78 (4.32)	24.68 (4.06)	24.22 (3.94)	24.28 (3.93)	23.42 (3.61)	24.64 (3.96)	23.91 (3.93)
Energy intake (Kcal)	1979.0 (536.08)	1925.3 (519.41)	1911.7 (532.84)	1876.4 (514.63)	2084.8 (590.63)	1930.4 (551.92)	2011.0 (561.45)

Annual weight change (kg)	0.20 (1.00)	0.24 (0.99)	0.14 (1.03)	0.64 (1.10)	0.34 (0.98)	-0.05 (1.12)	0.35 (1.00)
Corrected weight change (kg) ^c	0.40 (0.98)	0.44 (0.98)	0.36 (1.02)	0.85 (1.09)	0.45 (0.98)	0.15 (1.10)	0.51 (1.00)
School level (%)							
None	5.8	0.7	2.5	1.2	1.2	1.6	1.5
Primary	19.9	16.3	26.1	22.4	11.0	17.2	10.0
Technical/Professional	18.4	25.6	28.8	29.2	7.7	26.6	14.1
Secondary	27.2	25.1	21.4	24.4	35.6	24.8	30.3
University	23.9	27.1	18.8	20.7	41.0	26.9	36.2
Not specified	4.8	5.2	2.4	2.2	3.5	3.0	7.9
Alcohol consumption (%)							
0 g/day	18.6	9.1	13.9	10.8	7.9	10.7	9.5
1-6 g/day	44.5	42.1	38.9	42.8	37.6	40.3	44.2
7-18 g/day	25.7	31.6	26.2	28.7	29.7	30.1	31.6
19-30 g/day	6.8	9.1	9.9	9.3	14.2	10.1	8.3
31-60 g/day	4.0	7.3	9.3	7.3	9.5	8.0	5.7
>60 g/day	0.4	0.8	1.8	1.0	1.2	0.8	0.8
Physical activity (%)							
Inactive	21.3	14.3	17.2	14.0	15.1	13.0	17.9
Moderately inactive	33.5	30.2	28.4	26.5	33.5	27.9	34.2
Moderately active	22.1	22.7	18.8	18.2	29.3	21.7	25.8
Active	12.8	16.3	15.2	14.8	13.1	16.89	12.6
Missing	10.2	16.5	20.4	26.5	9.0	20.5	9.5

^a Statistical differences between longitudinal categories of smoking status were assessed using Kruskal Wallis tests for continuous variables and chi-squared tests for categorical variables

and the results obtained were highly significant ($p < 0.001$) for both men and women.

^b Never smokers at baseline who started and stopped smoking during follow-up

^c Weight change corrected for self-reporting applying the “Oxford correction equations” on self-reported weight at recruitment and follow-up.

Table 2. Estimates and corresponding adjusted means for the association between smoking and annual weight changes (in kg)^a. EPIC participants interviewed between 1992 and 2000 and after a follow-up of 5 years on average.

	Men (n=87,548)				Women (n=234,867)			
	Estimates		Adjusted means ^b		Estimates		Adjusted means ^b	
	β	95% CI	mean	95% CI	β	95% CI	mean	95% CI
Stable Never	ref		0.40	[0.33; 0.46]	ref		0.43	[0.35; 0.52]
Stable Former	0.05	[0.03; 0.07]	0.45	[0.39; 0.51]	0.01	[0.00; 0.02]	0.44	[0.36; 0.53]
Stable Current	-0.01	[-0.04; 0.02]	0.39	[0.32; 0.46]	-0.06	[-0.07; -0.05]	0.37	[0.29; 0.46]
Stable Never	ref		0.40	[0.33; 0.46]	ref		0.43	[0.35; 0.52]
Former ≤ 1 year at recruitment	0.27	[0.21; 0.34]	0.68	[0.59; 0.77]	0.13	[0.07; 0.20]	0.57	[0.46; 0.67]
Former 1.1-5 years at recruitment	0.08	[0.05; 0.12]	0.48	[0.41; 0.55]	0.04	[0.01; 0.06]	0.47	[0.38; 0.56]
Former > 5 years at recruitment	0.04	[0.02; 0.06]	0.44	[0.37; 0.50]	0.00	[-0.01; 0.01]	0.44	[0.35; 0.52]
Current < 20 cig/day at recruitment	-0.03	[-0.05; 0.00]	0.37	[0.31; 0.44]	-0.07	[-0.09; -0.06]	0.36	[0.27; 0.44]
Current ≥ 20 cig/day at recruitment	0.02	[-0.03; 0.06]	0.42	[0.34; 0.49]	-0.03	[-0.05; 0.00]	0.41	[0.32; 0.49]
Stable Current	ref		0.39	[0.32; 0.45]	ref		0.37	[0.29; 0.46]
Quitter	0.44	[0.36; 0.52]	0.83	[0.73; 0.93]	0.46	[0.41; 0.52]	0.84	[0.74; 0.94]
Stable Current	ref		0.39	[0.32; 0.45]	ref		0.37	[0.23; 0.46]
Quitter < 20 cig/day at recruitment	0.34	[0.24; 0.44]	0.72	[0.61; 0.84]	0.40	[0.34; 0.46]	0.78	[0.67; 0.88]
Quitter ≥ 20 cig/day at recruitment	0.73	[0.63; 0.82]	1.12	[1.01; 1.23]	0.72	[0.62; 0.82]	1.10	[0.96; 1.23]
Stable Never	ref		0.40	[0.33; 0.46]	ref		0.43	[0.35; 0.52]
Starter	0.01	[-0.08; 0.10]	0.41	[0.31; 0.52]	-0.03	[-0.07; 0.01]	0.41	[0.32; 0.50]

^a Estimates and adjusted means were obtained and derived from mixed-effects linear regression models adjusted for age, education, alcohol, physical activity, total energy intake, weight at recruitment and menopausal status in women. All models were based on more or less detailed tobacco variables having different reference categories and included all participants.

^b Corrected for self-reporting applying the “Oxford correction equations” on self-reported weight at recruitment and follow-up.

CI Confidence Interval

Titles and legends to figures

Figure titles

Figure 1. Difference in annual weight change (in kg) between quitters and stable current smokers in men after adjustment for age, education, alcohol, physical activity, total energy intake and weight at recruitment. EPIC participants interviewed between 1992 and 2000 and after a follow-up of 5 years on average.

Figure 2. Difference in annual weight change (in kg) between quitters and stable current smokers in women after adjustment for age, education, alcohol, physical activity, total energy intake, weight at recruitment and menopausal status. EPIC participants interviewed between 1992 and 2000 and after a follow-up of 5 years on average.

Figure 3. Difference in annual weight change (in kg) between stable former and stable never smokers in men after adjustment for age, education, alcohol, physical activity, total energy intake and weight at recruitment. EPIC participants interviewed between 1992 and 2000 and after a follow-up of 5 years on average.

Figure 4. Difference in annual weight change (in kg) between stable former and stable never smokers in women after adjustment for age, education, alcohol, physical activity, total energy intake, weight at recruitment and menopausal status. EPIC participants interviewed between 1992 and 2000 and after a follow-up of 5 years on average.

Figure footnotes

Figure 1.

Quitter means current smoker at recruitment who stopped smoking during follow-up while stable current smoker means current smoker at recruitment and at follow-up (reference group in this analysis)

Figure 2.

Quitter means current smoker at recruitment who stopped smoking during follow-up while stable current smoker means current smoker at recruitment and at follow-up (reference group in this analysis)

Figure 3.

Stable former smoker means former at recruitment and at follow-up while stable never smoker means never at recruitment and at follow-up (reference group in this analysis)

Figure 4.

Stable former smoker means former at recruitment and at follow-up while stable never smoker means never at recruitment and at follow-up (reference group in this analysis)